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EXAMINER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte IRIS ZIEGLER and JOHANNES BARTHOLOMAEUS

Appeal 2009-014562
Application 10/084,676
Technology Center 1600

Before TONI R. SCHEINER, MELANIE L. McCOLLUM, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL^{1, 2}

This is an appeal under 35 U.S.C. § 134 involving claims to an oral pharmaceutical formulation of tramadol and diclofenac. The Examiner rejected the claims as indefinite, anticipated, and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

¹ The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the “MAIL DATE” (paper delivery mode) or the “NOTIFICATION DATE” (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

² Oral Hearing waived.

Statement of the Case

The invention “relates to partially sustained-release, oral pharmaceutical forms of administration in which the active substance, tramadol, is present at least partially as a compound formed in situ which has a water solubility of ≤ 100 mg/ml, and to processes for their preparation” (Spec. 1 ¶ 0002).

The Claims

Claims 17 and 38 are on appeal. Claims 17 and 38 read as follows:

17. A sustained-release, oral pharmaceutical formulation of tramadol, comprising a compound of tramadol hydrochloride and diclofenac sodium, wherein said compound is formed in situ, said compound having a water solubility of ≤ 100 mg/ml, and wherein at least part of the tramadol and at least part of the diclofenac are released at the same rate.

38. A method for preparing an oral pharmaceutical formulation, the method comprising:
 mixing tramadol hydrochloride and diclofenac sodium to form a mixture;
 moistening the mixture; and
 repeating the above mixing and moistening steps and formulating the mixture under an energy input.

The issues

- A. The Examiner rejected claim 17 under 35 U.S.C. § 112, second paragraph as indefinite (Ans. 4-5).
- B. The Examiner rejected claim 17 under 35 U.S.C. § 102(e) as anticipated by Mauskop³ (Ans. 5-7).
- C. The Examiner rejected claim 38 under 35 U.S.C. § 103(a) as obvious over Mauskop (Ans. 8-9).

A. *35 U.S.C. § 112, second paragraph*

The Examiner finds that “the individual compounds, tramadol and diclofenac appear to be present in the claimed compound as identifiable compounds; secondly the formation of the claimed compound does not appear to involve the appearance of a new compound that is separate from the individual tramadol and diclofenac” (Ans. 5)

Appellants contend that the claim language

describes that “said compound” is formed *in situ* and that the compound has a water solubility of ≤ 100 mg/ml. Thus, the skilled artisan would readily understand that the claim is directed to a *compound* of tramadol hydrochloride and diclofenac sodium and not a simply mixture of these two ingredients . . . To read the language of claim 17 to cover a simple mixture of tramadol hydrochloride and diclofenac sodium improperly requires a complete disregard of the multiple recitations of the word “compound”

(App. Br. 4).

³ Alexander Mauskop, US 5,914,129, issued Jun. 22, 1999.

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that the use of the word "compound" renders claim 17 indefinite?

Findings of Fact

1. The Specification describes "the preparation of at least partially sustained-release, oral pharmaceutical formulations of tramadol, in which the sustained-release portion of the active substance is present as a [sparingly water-soluble] compound, formed in situ, of tramadol and another active substance and/or auxiliary substance with a water solubility of ≤ 100 mg/ml" (Spec. ¶¶ 9, 11).

2. In Example 1 of the Specification:

125 g of tramadol hydrochloride, 125 g of diclofenac sodium and 250 g of microcrystalline cellulose . . . were homogeneously mixed . . . for 10 minutes and then granulated with water in an amount sufficient for moistening. The sticky lumpy mass of granules was then extruded . . . with a 1.0 mm extrusion die. While the rods of extrudate were initially still extremely sticky, they changed in the course of the extrusion process to a very dry extrudate with insufficient plasticity for subsequent spheronization. The extrudate was moistened and granulated again. The resulting granules were extruded again . . . and the moist extrudate was then converted to round pellets of uniform size The pellets were dried in a drying cabinet at a temperature of approx. 50°C and fractionated into sieve fractions, $\geq 90\%$ of the pellets falling within the desired sieve class of 800 - 1250 μm .

(Spec. ¶ 54.)

3. “For the pellets produced above, the water solubility of the active substance tramadol from the *compound* formed in situ was found to be 0.36 mg/ml” (Spec. ¶ 56 (emphasis added)), and the release profile was as follows:

Time in min	Amount in mg released from 200 mg of pellets	
	for tramadol	for diclofenac
30	10	7
120	18	15
300	26	24
600	35	33

(Spec. ¶ 57.)

4. Dr. Iris Ziegler⁴ describes a series of experiments demonstrating the different properties of tablets “identical in size and shape and . . . made from identical amounts of the same raw ingredients . . . [which] differed only in their manner of processing” (Decl. 5).

5. Dr. Ziegler prepared three different compositions. First, section I(a) of the Declaration describes the preparation of tablets according to the process described in Mauskop (Decl. 2). Second, section I(b) of the Declaration describes the preparation of tablets according to the process of the instant application (Decl. 3). Third, section II(c)(i) of the Declaration describes preparation of the salt of Tramadol and Diclofenac (Decl. 7).

6. Exhibits A-E, which accompanied Dr. Ziegler’s Declaration show the results of Differential Scanning Calorimetry (DSC) thermal analyses of the three formulations of tramadol-hydrochloride and diclofenac-

⁴ Declaration of Dr. Iris Ziegler, dated December 14, 2006, and initially submitted in the present application on December 15, 2006 under the provisions of 37 C.F.R. § 1.132 (“Decl.”).

sodium, including the tablets of I(a), of I(b)(i), and a tramadol-diclofenac salt.

7. Dr. Ziegler concluded:

The different release profiles of the Tramadol and Diclofenac from the tablets of I(b) . . . compared to the tablets of I(a) . . . containing a mixture of Diclofenac-sodium and Tramadol-hydrochloride, are indicative of a significant difference in solubility and demonstrate that the Diclofenac and Tramadol must be present in a physical/chemical form which is different from a mixture The different differential scanning calorimetry results of the pellets of I(b)(i) produced according to the present invention compared to the tablets of I(a) containing a mixture of Diclofenac-sodium and Tramadol-hydrochloride . . . and particularly the endothermic peak at approximately 292°C which has no counterpart in the DSC of the crushed tablets of I(a), corroborate the presence of a different physical/chemical species in the product of the present invention which is not present in the tablets containing a mixture of Diclofenac-sodium and Tramadol-hydrochloride These results evidence that the product of the present invention contains an *in situ* formed compound of Diclofenac-sodium and Tramadol-hydrochloride which is not present in the tablets containing a mixture of Diclofenac-sodium and Tramadol-hydrochloride

(Decl. 9).

Principles of Law

“The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification.”

Miles Laboratories, Inc. v. Shandon Inc., 997 F.2d 870, 875 (Fed. Cir.

1993). “The purpose of claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not ‘indefinite’ simply because it is hard to understand when viewed without benefit of the specification.” *S3 Incorporated v. NVIDIA Corp.*, 259 F.3d 1364, 1369 (Fed. Cir. 2001).

Analysis

While we appreciate the Examiner’s concerns, we are not persuaded that the use of the word “compound” renders claim 17 indefinite. Appellants have provided specific evidence that at least three different physical entities can be formed using Tramadol and Diclofenac: a simple mixture as in Mauskop; a Tramadol/Diclofenac salt; and a third physical entity which is the inventive combination of Tramadol and Diclofenac (FF 5). Dr. Ziegler’s Declaration provides evidence that the three forms differ in at least some physical properties (FF 6-7).

Thus, while the physical entity of Claim 17 has not been described by its precise chemical structure, the issue is not whether “compound” is the best of all possible words to describe what is claimed. It may be that further research would show the physical entity to be a coordination compound, an inclusion compound, a sandwich compound, a clathrate, or some other form. The issue is whether one of skill in the art would understand what the word “compound” means when read in the context of the Specification.

We find that one skilled in the art would understand that, in this context, the word “compound” refers to physical entity, composed of tramadol hydrochloride and diclofenac sodium, formed in situ, with a water

solubility of ≤ 100 mg/ml, that is the product of the compounding process described in the Specification.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that the use of the word "compound" renders claim 17 indefinite.

B. 35 U.S.C. § 102(e) over Mauskop

The Examiner finds that "Mauskop discloses a combination of opioid analgesic and non-opioid analgesic to synergistically act to relieve pain (column 3, lines 47-54) and tramadol hydrochloride and diclofenac sodium are included in the list provided" (Ans. 6). The Examiner finds that the "property of a composition is not separable from the composition and how a composition is made has no patentable weight in a composition/product claim" (Ans. 6).

Appellants contend that the "different release profile and the different DSC spectrum obtained for the claimed compound show that the claimed compound is different from a simple mixture of the two active substances" (App. Br. 7).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that the composition of Mauskop is inherently the same as the composition of Claim 17?

Findings of Fact

8. Mauskop teaches that "[c]ompressed tablets may be prepared by compressing in a suitable machine the mixture of one or more analgesic, magnesium salt, stimulant, optionally an effervescing agent, and a pharmaceutically acceptable carrier" (Mauskop, col. 6, ll. 20-24).

9. Mauskop teaches non-opioid analgesics such as dichlophenac and opioid analgesics such as tramadol (*see* Mauskop, col. 3, ll. 1-8).

Principles of Law

Where ... the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on “inherency” under 35 U.S.C. § 102, on “prima facie obviousness” under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO’s inability to manufacture products or to obtain and compare prior art products.

In re Best, 562 F.2d 1252, 1255 (CCPA 1977) (citations omitted).

Analysis

The Examiner asserts that the Specification and claims are directed to a simple mixture of tramadol and diclofenac (*see* Ans. 7). There is no apparent dispute about Mauskop’s disclosure - Appellants and the Examiner agree that Mauskop discloses a simple mixture of tramadol and diclofenac (FF 8-9). However, the Examiner has failed to come to grips with the evidence of record which is consistent with Dr. Ziegler’s conclusion (and Appellants’ assertion) that there is “a different physical/chemical species in the product of the present invention which is not present in . . . tablets containing a mixture of Diclofenac-sodium and Tramadol-hydrochloride” (FF 4-7), and which has a substantially different solubility and release profile than a simple mixture of tramadol and diclofenac (*id.*).

In the instant case, the Examiner's initial action reasonably challenged Appellants to prove that the prior art differs from the claimed product. Appellants however, met that challenge, demonstrating with evidence in the Ziegler Declaration that the prior art products differ in several characteristics from the claimed product (FF 4-7). The Examiner has not rebutted this evidence, nor explained why the products would have been expected to be the same in spite of their different release profiles and different differential scanning calorimetry results.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that the composition of Mauskop is inherently the same as the composition of Claim 17.

C. 35 U.S.C. § 103(a) over Mauskop

The Examiner finds that Mauskop "discloses forming tablets by conventional method of compression and molding and specifically discloses that molded tablets can be optionally moistened with an inert liquid diluent" (Ans. 8). The Examiner finds that the "instant method comprises a moistening step which the prior art discloses. Repeating the mixing and moistening steps is an obvious variant of the method at the disposal of the person of ordinary skill in the art or to the skilled artisan whereby the steps are repeated as necessary for the production of the desired tablet" (Ans. 8).

Appellants contend that "the rejection fails to explain why the skilled artisan would be inclined to repeat the above mixing and moistening steps and formulate the mixture under an energy input as is required in claim 38" (App. Br. 9). Appellants contend that neither "Mauskop nor any other

evidence of record discloses or suggests the possibility that these steps might yield a compound as contemplated in the present application” (App. Br. 9).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that repeating the mixing and moistening steps would have been obvious over Mauskop?

Principles of Law

An invention

composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.

KSR Int’l Co. v. Teleflex Inc., 550 U.S. 398, 418 (2007).

Analysis

We find that Appellants have the better position. The Examiner acknowledges that “Mauskop does not describe repeating mixing and moistening steps” (Ans. 12). The Examiner has provided no evidence or reason why the ordinary artisan would have performed the steps of repeatedly mixing and moistening a mixture of tramadol hydrochloride and diclofenac sodium (as required by claim 38) when Mauskop does not teach or suggest this element.

Conclusion of Law

The evidence of record does not support the Examiner’s conclusion that repeating the mixing and moistening steps would have been obvious over Mauskop.

SUMMARY

In summary, we reverse the rejection of claim 17 under 35 U.S.C. § 112, second paragraph.

We reverse the rejection of claim 17 under 35 U.S.C. § 102(e) as obvious over Mauskop.

We reverse the rejection of claim 38 under 35 U.S.C. § 103(a) as obvious over Mauskop.

REVERSED

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